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ABSTRACT

The document presents a collection of articles about inhalant abuse. Article 1 presents findings on the psychophysiological effects related to the use of amyl or butyl nitrate as a "recreational drug." Article 2 suggests a strong association between chronic sniffing of the solvent toulene and irreversible brain damage. Article 3 warns about the possible effects of inhaling typewriter correction fluid. Article 4 further discusses the abuse of butyl nitrate and nitrous oxide (laughing gas) and mentions possible psychophysiological effects, number and age of users, frequency of use, variations in nitrous oxide formats, long-term effects, and government attempts to control inhalant abuse. Article 5 looks at research done on inhalant abuse, occurrences of volatile substances in common products, user motivation, administration and experience, pharmacology and toxicology, tolerance and dependence, and recommendations regarding the helping of abusers. The document concludes with an annotated bibliography of 30 books and articles about general inhalant abuse, and the abuse of nitrous oxide, amyl and butyl nitrate, and solvents. (LH)

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Inhalants

SP 015 303

Amyl nitrite: an old high comes back to visit

by Thomas P. Lowry, MD
Napa State Hospital
Imola, CA

There has been a dramatic increase in the number of individuals using amyl or butyl nitrite as a "recreational drug." This article reveals current findings on psychophysiological effects and what to do about presenting complaints.

It's been a long day in the emergency room. An excited school nurse has just sent in four third-graders who fainted on the playground after playing with one child's mother's "smelling salts." Next in the waiting room is a well-tailored young man with tracheal irritation: "My friend spilled a bottle of Dr. Bananas up my nose." Following him is a young woman who tells you, "My boyfriend and I did a lot of Locker Room and my head is killing me."

While you're unlikely to see all these problems in one day, they were all reported by different doctors in a recent survey of the 3,065 AMA-listed emergency room physicians in the United States. All the patients just described were affected by the old-time remedy amyl nitrite, and its cousin isobutyl nitrite. These two chemicals have become leading recreational drugs in this country, with annual sales of over 250,000,000 doses.

Why did the school children faint? Why does the woman have a headache? What are Dr. Bananas and Locker Room? A look at nitrite pharmacology will help.

Amyl nitrite is a volatile, highly flammable liquid. The basic pharmacologic action is relaxation of vascular smooth muscle. It has been used since 1867 in the treatment of angina pectoris; its beneficial action is not by direct effect on the heart, but rather by relaxing systemic arterioles, with a decrease in left ventricular work and a fall in blood pressure. Amyl nitrite is also used in differential diagnosis of heart murmurs, as an antidote for cyanide poisoning and in the early phases of cholecystitis.

Isobutyl nitrite has been little investigated. One hemodynamic study showed transient hypotension and tachycardia 30 seconds after inhalation, a response identical with the effects of amyl nitrite. With both amyl and butyl nitrite, blood pressure and heart rate returned to normal within 90 seconds.

But why are millions of people using volatile nitrites? Is there an epidemic of angina pectoris? Hardly. What has happened is a widespread discovery (or rediscovery) that volatile nitrites can be used to enhance the perception of social activities, dancing, for instance, but particularly sex.

Like many perception-altering chemicals, the social setting is important. A whiff of amyl nitrite, as used in clinical and diagnostic settings, is perceived as mildly unpleasant with feelings of dizziness, nausea, flushed skin and pounding heart. But in a setting of affection and passion, taken about 30 seconds before orgasm, there can be a strong enhancement of perceptions.

Users tell me the most remarkable things: "It's like being shot through the stars in a rocket. The orgasm is truly awesome. I can feel my whole body accelerate; my climax keeps building up and building up; all the rest of the world just disappears and it seems to go on forever. Words are no good to tell you how I get lost in my lover and the sensations. My inhibitions evaporate and almost every kind of sex seems possible and desirable. My whole body streams and throbs. In the center of my vision is The Flower, a bright yellow center with deep purple petals radiating out. With the right person, it's like a religious experience, ecstatic, transcendent."

I recently did a study of 240 male users of amyl and isobutyl nitrite; all respondents live in the San Francisco

Dr. Lowry is a medical consultant of the Office of Program Review in the Department of Developmental Services at Napa State Hospital and assistant clinical professor of psychiatry at the University of California at Davis.

The most common place for the use of the volatile nitrites is in bed, during lovemaking.

Bay Area. The average age was 30; the average user began about six years ago. Most of the men used the nitrites twice a week. When asked about sexual experience under the influence of the nitrites, 72 percent said there was increased intensity of feeling, 15 percent mentioned an apparently increased duration of orgasm and 20 percent said the nitrites facilitated sexual activity previously experienced as negative, such as fellatio and anal intercourse.

The dozen female users I queried reported similar responses, with the exception that several women said their orgasms were blocked by amyl nitrite: "I enjoy the sensations; my whole skin becomes sensitive; being kissed all over while sniffing amyl is like a wonderful dream, but I can't get off. I get right at the edge and then my orgasm slips away. It sounds funny, but sensuousness is all over my body but for me orgasm has to be focused." Most of the female respondents were in their 20's, but one, a college instructor age 45 had 26 years of experience with amyl nitrite. The women tended to use nitrites about half as often as the men in this study.

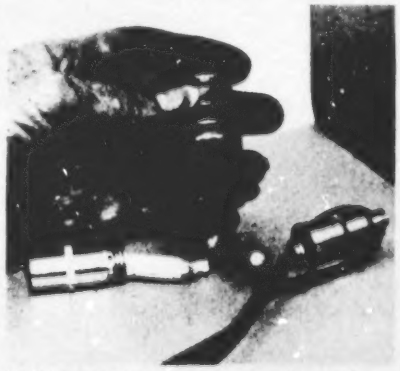
Where do users buy nitrites and how do they use them? Amyl nitrite, manufactured largely by Burroughs Wellcome and Eli Lilly, was a prescription drug until 1960, was sold over the counter for nine years and then was returned to the prescription list. It is distributed in 0.3 ml. glass ampules. To inhale the vapor, the ampules are crushed between the fingers. This makes a popping noise, which leads to the nickname "popper."

Isobutyl nitrite is used as an intermediate substance in manufacturing, but its widest market now is as a "room odorizer." It is not licensed or advertised as a drug and its biological effects are known mostly by word of mouth. The label of one brand states, "Danger. Excessive use may cause euphoria."

The purity of manufacture varies widely as does the list of trade names: Rush, Bolt, Locker Room, Bullet, Aroma of Man, Jac Aroma, Dr. Bananas, Cat's Meow, Satan's Scent, Hi Baller, Black Jac, Hardware, Heart On, Locker Popper, Ban Apple Gas, Toilet Water, Loc-A-Roma, Oz, Shotgun, and Cum.

The typical isobutyl nitrite container is a 12 ml. bottle with a screw cap, sold in an adult bookstore or boutique. Most users sniff the fumes directly from the bottle, but 32 percent of users prefer an inhaler, usually a metal device with a nozzle for insertion in one nostril while the other nostril is held shut. Most inhalers have a lanyard and can be worn around the neck. Users who enjoy nitrites while dancing wear the inhaler as a pendant while they disco.

The most common place for the use of the volatile nitrites is in bed, during lovemaking. Lovers may stay high during most of the proceedings, or confine their use to a deep inhalation as orgasm approaches. In a few seconds, the skin over the face, neck and shoulders turns hot and bright red, the pulse pounds and an altered state of consciousness arrives.



Volatile nitrites come in several forms for popular consumption. Above, the typical 12 ml bottle of isobutyl nitrite, a .3 ml gauze-wrapped ampule of amyl nitrite, and a disassembled metal inhaler with lanyard.

The neurophysiology of the nitrites is mostly unknown, but the usual explanation for the effects (peripheral vasodilation followed by hypotension followed by cerebral ischemia) is probably incorrect, since a social user may experience the same effects while lying flat on her back with her legs up in the air, which ought to facilitate venous return and enhance cerebral blood flow.

Studies in progress using scalp lead EEG and auditory evoked potential studies of the brain stem, suggest that the principal effects are midbrain, not cortical and are demonstrably transient.

The practicing physician, after learning of the uses of the nitrites will want to know if they present dangers to his patients. What is the clinical toxicology of these compounds?

A recent symposium summarizes current knowledge. One study sent a questionnaire to the 3,065 emergency room specialists and 213 forensic pathologists listed in the American Medical Association's computerized address system. Forty-seven forensic pathologists and 605 E.R. specialists replied. All the pathologists stated that they had never seen a patient whose death was attributed to isobutyl or amyl nitrite. Of the E.R. doctors, 592 had never seen a case of nitrite toxicity; the 13 who said they had seen toxic reactions described transient episodes of vascular headache, fainting or hypotension. The respondents had a combined total of 2,780 years of full-time E.R. experience.

Another study in the same symposium measured respiratory function using forced vital capacity spi-

rometry before and after the inhalation of an aerosol of the bronchodilator isoetharine. The spirometrist was unaware of the subject's history of tobacco, marijuana and/or isobutyl nitrite use. The study group whose members inhaled an average of four "poppers" a day for the past seven years (in itself an amazing record!) did not differ from a control (no "popper") group in age, height, weight, symptoms or spirometric function. The pulmonary health of the study group is all the more remarkable since their tobacco use was 500 percent greater than that of the control group and marijuana use was 1100 percent greater than that of the control group.

Parker studied five workers in an isobutyl nitrite bottling plant. They were exposed to moderately high concentrations of nitrite in the ambient air, 40 hours a week. No significant effects were noted on heart rate, blood pressure or levels of methemoglobin.

A questionnaire was sent to the Burroughs Wellcome Company (which has made amyl nitrite since 1924) and to Eli Lilly and Company (which has made amyl nitrite since 1913). Neither company has any reports of injury in its files.

The following Federal agencies have no reports on file of injuries from amyl, butyl and/or isobutyl nitrite: Alcohol, Drug Abuse and Mental Health Administration, Council on Environmental Quality, Consumer Product Safety Commission, Environmental Protection Administration, Food and Drug Administration, National Center for Health Statistics, National Highway Traffic Safety Administration, National Institute on Drug Abuse, National Institute of Health, National Institute for Occupational Safety and Health, National Technical Information Service and the Veteran's Administration.

The Department of Justice Drug Abuse Warning Network (DAWN) has surveyed 1,350,000 drug-related emergency room visits. Only 67 such visits were related to the volatile nitrites. Sixty of the patients were immediately released; there were no deaths. It is interesting to note that of all reported abuses of drugs, inhalants of every type (which consist mostly of spray paints and glues) constituted only four-tenths of one percent of all cases reported.

In my survey of over 250 users, 43 percent reported that on at least one occasion they had experienced headache following nitrite use, usually after "very heavy" use the night before. I have done a dozen in-depth interviews of amyl nitrite users; with this group, headache and respiratory irritation are totally absent. One woman, age 35, used ten ampules in an evening, trying to get "totally disconnected." She reported no ill effects. I suspect that the small number of unpleasant feelings reported by some users may reflect the impurities found in brands of isobutyl nitrite manufactured under poor quality control.

Overall, the record of consumer safety is far better with the volatile nitrites than with aspirin and/or alcohol. There are no verified deaths and no permanent injuries reported for these nitrites. Future studies may show harm, but since 1915 over a billion have been consumed without a confirmed instance of serious harm. In summary, physicians will hear more of the recreational use of the volatile nitrites. The most likely presenting complaints will be headache or dizziness. No specific treatment is needed, other than lying down and perhaps taking two aspirin. Rest and abstinence seem to cure all nitrite symptoms. ■

Are poppers really safe?

Not everybody is sure they are. While the possible, immediate side-effects appear to be well-known and minor — headaches, dizziness, nausea, fainting — some gaps do exist in our knowledge about these mind-altering drugs. "At this time, there is no great evidence of serious, organic symptoms due to the use of butyl nitrite," asserts Dr. Richard Phillipson, special assistant for scientific and medical affairs at the National Institute for Drug Abuse. "However," he warns, "use in combination with other substances could possibly be hazardous to health, and the possible ill effects of long-continued use has yet to be seen."

Other experts have warned about potential ill effects on the cardiovascular system, especially for those individuals with latent cardiac disease. The controversy about the volatile nitrites is beginning to spread. Butyl nitrite was made a prescription drug in Georgia and banned in Connecticut. Because of the uncertainties surrounding continued use of these inhalants, one of the major pharmaceutical firms which manufactures them was responsible for initiating action to change their OTC status.

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Irreversible brain damage revealed in people sniffing toluene

By Wendy Wright

TORONTO — A strong association between chronic sniffing of the solvent toluene and irreversible brain damage has been shown by Addiction Research Foundation (ARF) scientists in the largest, most comprehensive study of its kind.

The findings are important, not only for young abusers, but also for industrial workers chronically exposed to substances containing toulene, the research team says.

The ARF study links long-term use of toluene, which most abusers choose to sniff, to short-term memory loss, and fine-motor defecit.

The cerebellum appears to be the part of the brain most sensitive to toluene. Brain scans show the cerebellum being "eaten away."

Toluene is cheap and easy to obtain. In highly-concentrated form, it's found in contact cement and contact cement cleaner. Gasoline and paint thinners contain toluene in lesser concentrations.

Luis Fornazzari, neurologist with ARF, and a member of the team that did the study, says the number of people deliberately abusing toluene is low.

However, the effects are critical, considering abusers are generally quite young, and their bodies still developing. The fact that neurological damage is irreversible for chronic users makes the effect alarming.

Consistent with the cerebellum damage, the researchers found the subjects in the study had trouble with coordination — especially fine motor coordination. Some had great difficulty eating and writing.

The ventricles and sulci (grooves) on top of the brain were observed to be enlarged, indicating further atrophy around these spaces. The marked loss of short-term memory seen in the subjects is related to destruction in this area of the brain, suggests the study team.

Until now, research on the effects of solvents concentrated on the acute effects because the number of abusers who sniff for long periods of time are relatively low compared to those who try it occasionally.

(The study team presented their findings to a seminar on solvents sponsored by the ARF's School for Addiction Studies. Dr Fornazzari was also to present the findings at the end of April at a meeting of the American Academy of Neurology in Washington.)

Manufacturers should look for toluene substitutes, says Adrian Wilkinson, ARF scientist. **p2**

Reprinted from *Drug Survival News*, 10(5), April 1982.

White Out Warning Label Proposed

KINGMAN, Az.—A coroner's report linking the death of a teenage girl to inhalation of typewriter correction fluid has led manufacturers of Liquid Paper to consider warning labels for the product.

The Gillette Company, makers of the quick-drying opaquing fluid Liquid Paper, commonly known as "white out," announced that it will reevaluate the potential for toxic reactions caused by inhalation of the product. According to a company spokesperson, warning labels stating that the product is "non-flammable" and "non-hazardous" when used as directed, were eliminated from Liquid Paper packages in early 1981.

The fluid, which contains the chlorinated solvent, trichloroethylene, is believed to produce a state of giddiness and intoxication when inhaled and is increasingly identified as a common, easily-obtainable intoxicant among adolescents.

Gillette recently lost a settlement in connection with a 1977 death attributed to white out abuse, and federal authorities believe that as many as a dozen teenage fatalities since 1975 may have been caused by inhalation of the fluid.

Inhalants: Quick Route To Danger

Inhaling certain substances to get "high" has been risky all the way back to antiquity, and is no less dangerous in modern times. Adding to the problem today are a couple of substances that have enjoyed a certain amount of social acceptance: butyl nitrite, sold as a "room odorizer," and nitrous oxide, better known as "laughing gas." But there's nothing laughable about the hospital trip that may result from using these and other inhalants.

by Annabel Hecht

In 1978 over 150 people in this country died as a result of inhaling volatile substances, such as gasoline, spray paint, paint thinner, or transmission fluid. About 1,800 more required emergency room treatment. These deaths did not occur because of accidental exposure in the workplace. The substances were deliberately inhaled for their intoxicating effects, with no appreciation for the dangers involved.

While FDA does not have regulatory authority over all volatile substances, the Agency is very much concerned about the increasing abuse of two inhaled substances that are under its control. One is butyl nitrite, a substance being sold under the guise of a "room odorizer." The other is nitrous oxide, a gas with a variety of legitimate uses, including use as an anesthetic. It is sometimes called "laughing gas."

Because the respiratory system provides a quick route to the bloodstream, inhaling a volatile substance is like having it injected into the body. The effect can be immediate with loss of consciousness, heart irregularities, or even death. After a time, those who inhale substances such as solvents may develop organic brain syndrome, a condition characterized by loss of muscular coordination, lethargy, irritability, confusion, or disorientation. Inhaling volatile substances also can lead to peripheral nerve injury, and liver and kidney disease. Long-range effects, which may not show up for 10 to 30 years, include an increased risk of developing cancer as well as genetic changes.

Despite the world-wide extent of inhalant use and abuse, it has been only in the past 30 years that social scientists have studied this phenomenon in the United States. One of the early episodes reported involved a local outbreak of gasoline sniffing in Warren, Pa., in 1951. Further public attention was focused on inhalant abuse in the 1960's when adolescents took to sniffing the glue they were using to make model airplanes and cars. The popularity of the habit was intensified, some observers say, by sensational press and community campaigns against it.

Completely overlooked in the furor over glue sniffing was that adolescents also were sniffing an assortment of other commercial solvents, a variation of drug abuse that probably got started in the late 1950's. Swirling in their heads were the vapors from contact cements, paints, lacquers, drycleaning fluids, transmission fluids, liquid waxes, shoe polish, lighter fluids, nail polish removers, degreasers, and refrigerants.

Aerosols came along in the sixties, starting with glass chillers and vegetable nonstick fryer sprays. Every type of aerosol has been abused, including cold weather car starters, air sanitizers, window cleaners, furniture polishes, insecticides, disinfectants, spray medications, deodorants, hair sprays, and antiperspirants. Clear lacquers and gold and bronze paint sprays also are popular among sniffers.

The seventies has seen a surge in the abuse of nitrous oxide—mainly by health professionals and college-age youth—and of butyl nitrite, close chemical kin to a drug used to treat symptoms of angina pectoris.

Just who is sniffing this array of substances? Statistically their numbers are small. The National Institute of Drug Abuse (NIDA) estimates that about 7 million people over the age of 12 have experimented with or are chronic users of inhalants. In contrast, 42 million have tried or used marijuana. However, experts in the drug abuse field believe that many inhalers just don't get counted. For instance, those most likely to abuse industrial solvents, often school dropouts or truants, aren't likely to be covered in school surveys of drug abuse. In the past, surveys frequently did not include questions about inhalants, or they lumped everything under "glue sniffing." In addition, inhalant users seldom seek medical attention for problems related to their sniffing habit, so they don't often show up in emergency room reports.

The largest concentration of inhalant users appears to be among young adolescents. One study of high school students nationwide showed that 12 percent of the class of 1978 had sniffed something at some time in their lives. Around 2 percent were current users. These figures represented a slight increase over the previous 2 years. More boys than girls indulge in sniffing, but the gap between their numbers is closing.

In contrast to users of illicit drugs, most of whom got their start in the last 3 years of high school, a majority of inhalant users had their first sniff before they got to the 10th grade, according to the survey of the class of 1978. It was once thought that this adolescent interest in sniffing glue or other substances fades as the sniffer matures. Actually, recent studies suggest that as they grow older, those who indulge in this type of substance abuse start using other drugs but only partially cut down on their inhalant use. Current interest in nitrous oxide and butyl nitrite among college students also suggests that inhalant

use is not just "kid stuff."

Early research pictured the typical sniffer of industrial solvents as poor and frequently Hispanic. While it remains more prevalent among the poor, inhalant use today does cut across socioeconomic lines, researchers have found. Inhalants are used more often in rural areas than in the city, studies have shown.

Adolescents bent on getting "high" choose volatile substances for a number of reasons. The intoxicating effect is immediate, though not long lasting. What they sniff is inexpensive, readily and legally available, and often found in the home or workplace. Compact packaging makes items such as glue or nail polish remover easy to slip into a pocket or purse. The dangers of sniffing—including the potential danger of death—are ignored.

The health problems of inhalant users have not been studied systematically. What is known of the damage users cause themselves comes from a limited number of medical histories and from studies of people exposed to solvents on the job. Such studies have shown, for instance, that chronic exposure to benzene, a component of some solvents and of gasoline, can cause leukemia and severe anemia. Glue and contact cement contain n-hexane which can damage the nervous system and cause numbness, loss of touch sensation in the feet, and limb weakness. Ketones in rubber cements, printing ink, and paint can cause similar nerve damage. This impairment may show up sooner after exposure to ketones than after exposure to n-hexane.

Methylene chloride, used as a solvent in spray paints and thinners, converts to carbon monoxide in the body, which interferes with the distribution of oxygen. Chloroform, trichloroethylene, and halothane all have the potential to cause cancer if used repeatedly for recreational purposes. Death has been associated with exposure to household cleaning fluids containing trichloroethylene and methylchloroform.

Perhaps some of the greatest inhalant tragedies in the past were the deaths of many youngsters who sniffed the Freon aerosol propellants in such products as vegetable frying pan spray. It is estimated that as many as 700 deaths may have occurred in the 1970's from inhaling all types of aerosols. In many of these cases sudden death was caused by heart irregularities brought on when sniffing was followed by vigorous exercise.

Not to be overlooked in the list of the ill effects of inhalant abuse is the damage to the psyche. Youngsters who get an early start as sniffers may be paying a high price in terms of their psychological as well as their physical development. Dealing with problems through solvent fumes is poor preparation for coping with the normal stresses of life. Furthermore, youngsters who abuse solvents are among the heaviest drug users.

The picture that emerges of the abuse of butyl nitrite and nitrous oxide is much different than that of industrial and commercial solvents.

Butyl nitrite came on the drug abuse scene in the early 1970's. It is closely related chemically and pharmacologically to amyl nitrite, a prescription drug that has been used in treatment of angina pectoris (pain related to heart ailments) since 1867. Butyl nitrite was investigated for drug use in 1880, but has never been used clinically to any extent.

When amyl nitrite was made an over-the-counter drug in 1960, it became a prime candidate for abuse. Called "poppers" because of the sound made when the mesh-covered glass vials or ampules were crushed prior to inhalation of the fumes, these drugs gave the user a quick "high."

FDA reclassified amyl nitrite as a prescription drug in 1969 and butyl nitrite became more readily available. First popular in homosexual communities, butyl nitrite is now used both as a sexual stimulant and euphoriant in heterosexual circles. Sold as a "room odorizer" or "liquid incense" under a variety of names that are suggestive of its odor--Banapple Gas, Locker Room, Rush, Jac Aroma, Satan's Scent, Locker Popper—butyl nitrite is available in novelty stores, some record stores, and "head" shops that cater to drug-oriented youth.

How many people are using butyl nitrite is difficult to say. It is estimated, on the basis of sales data published in the press, that 4 to 10 million vials of the drug are sold each year. Primary users are older teenagers and young adults of both sexes.

The most recent survey of high school students made by the National Institute of Drug Abuse reveals that 1 out of every 9 seniors has tried butyl nitrite; 1 out of 40 used it in the month just prior to the survey; and about 1 out of every 1,000 students uses it every day.

FDA is aware of two deaths from butyl nitrite. One death was attributed to ingestion of the substance. Users generally experience headaches, dizziness, perspiration, and flushing of the face. Less common reactions include nausea, vomiting, and fainting. There is a risk that over a time the heart and blood vessels could be damaged. Inhaling nitrite could be fatal to people with heart disease.

Nitrous oxide is even older than amyl and butyl nitrite. Discovered accidentally in 1773 by Joseph Priestly, nitrous oxide was one of the first volatile substances to be abused. In the 18th and 19th centuries "ether frolics" and demonstrations of "laughing gas" were common parlor games among the upper classes. The fact that the participants in these events were feeling no pain eventually led to the realization that these gases have a legitimate use in medicine. Ironically, Dr. Horace Wells, the man who introduced nitrous oxide to dentistry in 1844, died as a result of chloroform abuse.

Today, nitrous oxide has a number of commercial uses

including that of general anesthetic, particularly in dental offices; propellant to manufacture whipped cream; rocket fuel; and leak detector. Only the first two package forms are believed to be abused.

Abuse of nitrous oxide as an anesthetic has a long history. One medical historian has recounted cases of misuse of the gas by American medical students in the late 19th century.

How many people in the health professions today may be abusing nitrous oxide is not known, but reports in the medical literature and other sources suggest that anesthesiologists, doctors, nurses, dentists, and inhalation therapists are among those who do.

When nitrous oxide is a propellant for making "whipped cream," it is either in an aerosolized spray can where it is considered a legitimate food additive, or in a small 8-gram metal cylinder, intended to be used with a dispensing machine. These cylinders are popularly called "Whippets," since that is the brand name of one version of this product. The cylinders are being purchased—often at "head shops"—by young people, particularly college students, who have no intention of whipping anything edible. Paraphernalia used with the cylinders include balloons from which the gas is inhaled. One man has come up with a device called a "Buzz Bomb," which combines the nitrous oxide cylinder with a pipe for smoking.

The number of young people abusing this form of nitrous oxide is not known, although an article in the September 12, 1978, issue of ESQUIRE magazine claimed that production of Whippets had tripled in the last few years and many legitimate users were unable to get supplies. FDA has not been able to verify these statements. An informal survey of a number of States, made by the Agency last year, seems to indicate that nitrous oxide abuse by young people is not a major problem.

Damage to health from abuse of nitrous oxide is a problem, however. Death can result if the gas is inhaled with insufficient oxygen. Abuse of the gas over long periods of time can result in nerve damage, including loss of balance, leg weakness, tingling, and numbness in the fingers and toes. Shortness of breath, nausea, variations in heartbeat, and hearing loss also have been reported as side effects of nitrous oxide abuse. Studies of health professionals who are exposed to the gas in their work—dentists, dental technicians, anesthesiologists—have shown that these people have an increased risk of kidney and liver disease, spontaneous miscarriages, and other serious health problems.

"Doing something" about the small but persistent problem of inhalant abuse is not simple, since the range of products abused is large and patterns of abuse differ in various community and ethnic groups. Much more needs to be learned about the abusers, particularly in high risk groups. To fill some of these gaps in understanding inhalant abuse, the National Institute of Drug Abuse is funding research in such areas as laboratory testing of inhalant chemicals and studies of the cause and extent of the problem in different ethnic groups.

Controlling the abused products is one approach in controlling inhalant abuse. Obviously it would be impossible to ban industrial solvents that serve a useful purpose, especially since those sniffing these substances will simply turn to something else. However, other steps can be taken such as the addition of oil of mustard to airplane glue to make it smell bad, a move made voluntarily by glue manufacturers.

Warnings on labels is another way to stop product abuse. FDA took this step in 1975 to curtail abuse of nonstick frying pan sprays. When it was determined that aerosol cooking sprays were food additives within the Agency's jurisdiction, FDA called for the following warning on such product containers:

> "Warning—Use only as directed. Intentional misuse by deliberately concentratin g and inhaling the contents can be harmful or fatal."

This regulation became effective May 30, 1976. Since then chlorofluorocarbons, the aerosol propellant responsible for the deaths of young sniffers, has been banned from most consumer spray products because of its effect on the ozone layer in the atmosphere.

The labeling of hazardous household products, such as adhesives, paint thinners and removers, lighter fluids, cleaning solvents, lacquers, and aerosols containing volatile organic solvents is regulated under the Federal Hazardous Substances Act, now administered by the Consumer Product Safety Commission (CPSC). Hazardous products must bear a label that identifies any recognized hazardous substance in the product, the nature of the hazard, and warnings or cautions and first aid instructions. Additional warnings are required for the products that present a particular hazard. For instance, volatile organic solvents, such as toluene, xylene, and petroleum distillates that may be aspirated into the lungs must be labeled "Danger—Harmful or Fatal if Swallowed. If swallowed do not induce vomiting. Call physician immediately."

Even though glue-sniffing was popular at the time the Hazardous Substances Act was being written, the new law did not take into account the potential for deliberate abuse or misuse of household products. Thus, the act cannot be used to make deliberate solvent inhalation an offense or to take regulatory action against a manufacturer or a product that is deliberately abused.

As for butyl nitrite, manufacturers of the so-called room odorizers follow the CPSC labeling requirements to the letter. Despite extensive labeling and warnings such as "Avoid prolonged breathing of vapor," sales and abuse have not diminished. It would have to be proved that injury or illness occurred under recommended conditions of use—that is, as a room odorizer, before CPSC could take additional regulatory action.

Under the Toxic Substances Control Act, administered by the Environmental Protection Agency (EPA), manufacturers are required to submit information on substances that present "substantial risk of injury to health or environment" to the EPA Administrator, who is authorized to regulate any substance he determines to present "unreasonable risk." No information has been submitted by manufacturers of butyl nitrite.

FDA has been aware of the recreational use and abuse of butyl nitrite for several years and is exploring what course of action can be taken to halt this abuse. A key issue is whether butyl nitrite is a drug within the meaning of the Food, Drug, and Cosmetic Act. Determining whether it qualifies depends on how it is labeled.

To FDA, labeling includes not only the material printed on or fixed to the container, but other written,

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printed, or graphic material. This material does not necessarily have to accompany the product through the channels of interstate commerce to be considered labeling.

A butyl nitrite product properly labeled as a room odorizer would not be considered a drug, even though the person who bought it did so to get "high." However, if the manufacturer or distributor suggests in labeling that the product is an aphrodisiac or euphoriant, the product could be regulated as a drug.

In the meantime, many U.S. communities are seeking to impose legal bans or at least to limit the sales of this product to adults. Georgia and Connecticut, for example, have established controls on odorizer sales, and Houston, Tex., has banned their sale to minors.

Nitrous oxide as a medicinal gas is regulated as a prescription drug by FDA and many of the States. Nitrous oxide as a whipped cream propellant is regulated by FDA as a food additive. Where the 8-gram cylinders fit is not so clear. As in the case of butyl nitrite, the Agency is examining the options for controlling nitrous oxide abuse. Early this year a meeting was held with manufacturers of the gas to discuss steps that could be taken on a voluntary basis. Changes in labeling on nitrous oxide containers are being considered. Materials also are being prepared to alert the medical community to the danger or inadvertent or deliberate exposure to this gas.

State and local governments are also concerned about nitrous oxide abuse. Legislatures in at least two States, New Jersey and Pennsylvania, have introduced bills that would restrict use of the gas. In Oregon, all manufacturers and distributors are being licensed by the State pharmacy board and inspected annually to make sure nitrous oxide tanks are properly labeled. Records of registrants are being checked to verify legal sales. The Cincinnati city council debated, but did not ban the 8-gram cylinders. The Kansas City, Mo., Liquor Control Agency adopted a resolution prohibiting the use of nitrous oxide machines in bars.

Whatever regulatory steps eventually are taken, FDA cautions those who have access to nitrous oxide to use it only as the manufacturer intended. Nitrous oxide is a safe anesthetic in the hands of trained medical and dental personnel and an effective aerosol propellant. But experience now proves that abuse of nitrous oxide is no laughing matter.

Annabel Hecht is a member of FDA's public affairs staff.

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INHALANT ABUSE

By Marshall Werner

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Volume 5, No. 2 of The PharmChem Newsletter was devoted to the subject of the inhalation of volatile substances. The following article elaborates on the previous information and presents the results of recent research.

The early 1960's phenonmenon of "glue-sniffing" in the United States received substantial media attention. Nitrous oxide ("laughing gas") and amyl nitrite ("poppers") were included in public reports about inhalant abuse. Given the recent absence of media attention, one might hypothesize this type of drug abuse to be just a fad. It is true the abuse potential of nitrous oxide and other anesthetic agents (chloroform, ether, etc.) has been limited due to industrial and medical monitoring; however, recent research indicates an increase in the abuse of amyl and butyl nitrite, solvents and aerosol propellants. Mexico, Canada, Sweden and Japan have also reported cases of inhalant intoxication, and even in the isolated villages in Manitoba gasoline sniffing is a serious problem (Boeckx and Cooding, 1978).

Research has revealed that a broad spectrum of substances including shoe polish, fingernail polish remover, lacquer thinner, metallic spray paints, and vegetable lubricants for cookware have been inhaled for their intoxicating effects. Inhalant abuse encompasses three groups of substances: "organic solvents, either pure or in combination with other nonvolatile ingredients, hydrocarbon mixtures such as lighter fluid and gasoline, and aerosol propellants" (Hayden et al., 1976). Table I illustrates the diversity and ubiquity of these inhalants (page 2).

EXTENT OF USE

It is difficult to assess the true number of inhalant abusers since: 1) Abusers are usually brought to the attention of juvenile authorities when they participate in some sort of anti-social behavior such as shoplifting, public intoxication, truancy, or the destruction of property. This could result in the over-representation of a restricted population. 2) The wording of survey questions is inconsistent. (For example, in the 1972 National Survey the inhalant reference was worded "Glue or other things you breath in"; the 1974 survey included a reference to "other inhalants[s]" in addition to glue. It was not until the 1976 and 1977 surveys that references to "...things like gasoline, some aerosols, nitrous oxide, amyl nitrite which is also called 'poppers' and other solvents" were included [Abelson et al., 1977]). 3) It is difficult to obtain such self-disclosive material from juveniles suspicious of interviewer motivation when punitive measures, parental or judicial, may be anticipated.

Previous studies have reported inhalant abuse almost exclusively among juveniles, usually in the pre-teen to late teen years, with some as young as seven to eight years old (Press and Done, 1967). Adult use is reportedly infrequent, however, a slight increase (1.6%) is reflected in the National Surveys from 1972 (2.1%) to 1977 (3.7%). Adult use of inhalants within the past month for the same period has remained at less than 0.5% (Abelson et al., 1977). Inhalant abuse among adults evidently is limited to those in prisons and other institutions where alcohol and other drugs cannot be obtained (Press and Done, 1967).

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TABLE I
OCCURRENCES OF VOLATILE SUBSTANCES*

COMPOUNDS	Anti-freeze	Gasoline	Paint Thinner	De-greaser	Windshield Washers	Adhesives & Rubber Cement	Model Cements	Aerosol Sprays	Spray Shoe Polish	Room Deodorants	Foam Dispensers
ALCOHOLS											
Methanol	X		X		X						
Ethanol			X				X	X			
Isopropanol	X		X	X			X	X	X		
ESTERS											
Ethyl acetate			X								
n-Propyl acetate			X								
n-Butyl acetate				X							
KETONES											
Acetone			X				X				
Methyl ethyl ketone			X	X							
Methyl butyl ketone			X								
AROMATIC HYDROCARBONS											
Benzene		X		X		X					
Toluene		X	X	X		X	X	X	X		
Xylene		X	X	X		X	X	X			
Stryene						X	X				
Napthalene		X	X			X					
ALIPHATIC HYDROCARBONS											
n-Hexane		X				X	X				
n-Heptane		X	X			X					
ANESTHETICS											
Methylene chloride			X	X							
Trichlorethylene				X							
Tetrachloroethylene				X							
Nitrous oxide											X
**"FREONS"								X			
ALIPHATIC NITRITE											
Isoamyl nitrite										X	

*Source: Couri, Daniel, Introduction [Pharmacology and Toxicology]. In: *Review of Inhalants: Euphoria to Dysfunction*, Sharp, C.W., and Brehm, M.L., eds. Pub. No. ADM 77-553. Department of Health, Education, and Welfare, 1977.

**Ed. Note: "Freon" is the trademark for the fluorocarbons: trichlorofluoromethane (FC 11), dichlorodifluoromethane (FC 12), dichlorotetrafluoroethane (FC 114).

The results of recent research on the prevalence of inhalant abuse are presented in Table II (page 3). According to the results of the 1977 National Survey, about one in eleven (9%) of the twelve to seventeen year old respondents had inhaled a solvent for intoxicating purposes at least once. This represents a slight increase (0.9%) over the 1976 survey of ever use. Less than one percent (0.7%) of the twelve to seventeen year old respondents in the 1977 National Survey reported use within the past month (Abelson et al., 1977).

Adolescents involved in a 1974/75 New York State Survey (as cited in Stephens et al., 1978) had a 3.8% lower incidence of "ever use" of solvents than those in the 1977 National Survey. Although the percentage of current users was more than twice that of the National Survey, it is a comparison which requires modification due to the differences in definitions of "current use": use within the current month in the National Survey; use within the last six months in the New York State Survey.

The results of the specific intensive investigations conducted by Padilla et al. and Goldstein in 1975 may be reflective of a more reliable estimate of the actual problem of inhalant abuse, especially among minority youths. The Padilla interviewers were members of the Mexican-American communities surveyed; Native American law and graduate students conducted the interviews of the Pueblo students in New Mexico.

In both studies the rate of ever use and current use is significantly higher in comparison to the National Surveys (see Table II, page 3). Almost three times as many Mexican-

American adolescent youths and slightly less than two times as many Pueblo students had tried inhalants as had those in the 1977 National Survey. More youths in the Padilla and Goldstein studies reported current use within the past month (within the past week in the Padilla study) than their nationally surveyed counterparts as having *ever* attempted inhalant intoxication.

Interestingly, in contrast to earlier findings of an almost ten to one boy/girl user ratio reported in Press and Done (1967), the Goldstein study reported almost twice as many female users than male users (65% female; 35% male) although the sample was evenly distributed among both sexes. Goldstein ascribes this disparity to the cultural bias against female alcohol consumption.

TABLE II – RECENT SURVEYS OF INHALANT ABUSE

INHALANT USE	Abelson et al., 1977 National Surveys (age 12-17 yrs) 1974	1976	1977	Stephens et al., 1978 New York St. Students 1974	Goldstein, 1978 Pueblo Students 1975	Padilla et al., 1976 Mex.-Am. Adolescents 1975
EVER USE (one or more times)	8.5%	8.1%	9%	5.2%	17.2%	25%
CURRENT USE (in past month)	0.7%	0.9%	0.7%	1.9%*	13.9%	13.1%**

* last 6 months
** in past week

USER MOTIVATIONS

Unlike the psychedelics, cocaine, or any of the other recreationally used drugs, there is nothing exotic or mystical attributed to the abused inhalants. Why do individuals indulge in inhaling such substances as lacquer thinner, shoe polish, deodorants, or metallic spray paints in view of the serious health hazards posed by such use? Dr. Sidney Cohen of the Neuropsychiatric Institute at UCLA (1979) cites the following reasons, given by users, for involvement in inhalant intoxication:

- Peer influences tend to control the materials desired. Frequently sniffing is done in groups where the leaders will determine what type of intoxicant will be used (Hofmann and Hofmann, 1975). Results from the New York State Survey (Stephens et al., 1978) indicate a possible correlation between peer pressure and solvent use, the chronic users reporting the greatest amount of peer pressure.
- The inexpensiveness of most solvents is a significant factor due to the low-socioeconomic backgrounds of most users. Dr. Cohen (1978) states: ". . . even if solvents are not the preferred intoxicant, they are the most economically feasible . . . A 75-cent can of varnish remover can intoxicate more people than a gallon of cheap wine" (p. 10).
- Easy Availability: Little suspicion is generated by a teenager buying a hobby kit, wax stripper, or other household items which contain solvents. S/he could be interested in building the model or on an errand for her/his parent. As evidenced by the National Institute on Drug Abuse (NIDA) funded "Summary of Exploratory Study of Inhalant Use and Treatment" (1977), there is a correlation between accessibility and preference. The favored product in three of the eight areas cited was the one manufactured in the same areas.
- Convenient packaging allows the user to remain inconspicuous to school and juvenile authorities. A tube of glue can be easily hidden in a pocket. It also makes shoplifting easier.
- Mood Enhancement: Many users report a feeling of well being or euphoria while under the influence of inhalant intoxication, providing a refuge from the exigencies and responsibilities of daily life. Korman (1977) cites "boredom or idleness" as factors leading to solvent abuse. Stybel et al., (1976) recommend the establishment of community recreational programs as a constructive approach to eliminating adolescent ennui.
- The effects of solvent sniffing are experienced within seconds, producing a "high" which lasts approximately five to fifteen minutes (Prockop et al., 1974). The rapid high of inhalant intoxication without the ensuing hangover produced by alcohol makes it a desireable choice over alcohol inebriation (Cohen, 1978).
- The Legal Hassles: Although little concern about the legality or illegality of intoxicating substances is expressed by users (Cohen, 1978), the legal consequences of being caught with glue or other solvents are minimal compared with other frequently abused drugs like marijuana, LSD, or cocaine. According to Gellman (1978), "Penalties for violations vary from state to state from a minimum of $50 or five days to $1,000 or a year in jail" (p. 66). In addition, the ethics of such legislation enter into question since most violators are minors.

The afore-mentioned motivations suggest two user profiles: the experimentor, one who tries solvent intoxication once or twice at the suggestion of peers but does not continue to indulge in the practice (for many youths solvents may be the first substance of abuse other than alcohol); and the chronic user, one using the experience to escape. The escape may be from an environment of poverty, parental abuse or neglect, or simply from boredom.

ADMINISTRATION AND EXPERIENCE

The method of administration varies according to the inhalant used. Hydrocarbon sniffers surveyed by Stybel et al. (1976) preferred the "bagging" technique to other modes such as sniffing soaked rags, cotton, tissues, or from a cup filled with the substance. The authors warn of the danger associated with this method "... due to the tendency of sniffers to inhale carbon dioxide fumes along with the hydrocarbon gases" (p. 352). "Huffing", inhalation through the mouth, is another method utilized, especially when the inhalant used may irritate the nasal membranes if sniffed. The use of a "flute", fashioned from paper and enveloping material saturated with the substance, has also been reported (de la Garza Gutierrez, et al., 1978a).

Generally, about one third of a tube of glue or adhesive is squeezed into a bag; about an ounce of liquid solvent will thoroughly saturate a rag which can then be placed over the mouth and/or nose, or placed in a bag. Some users prefer to heat the liquid solvents in order to increase the vapor concentration. Hofmann and Hofmann (1975) describe methods used for aerosol particulate matter separation from propellant gases: the aerosol can be sprayed into a bag or balloon, the particulate matter adhering to the sides; the aerosol can be activated in an upside down position; cloth rags can be placed over the mouth or nose as filters. Less cautious users sniff directly from the original containers or add the solvents to carbonated beverages; their aerosol using counterparts eschew pre-filtering.

The effects of inhalant intoxication differ; some individuals report visual and audio hallucinations while others report only a vague floating sensation. Symptoms are similar to those induced by alcoholic intoxication. Dizziness, giddiness, incoordination, euphoria, drowsiness, and delusions of omnipotence are frequently reported by users (Press and Done, 1967). The duration of the intoxication varies according to the potency of the inhalant and the frequency of inhalation. Usually the action lasts from five to thirty minutes, however, it can be extended by repeated sniffing episodes throughout the day. As with other recreationally used drugs, the environment and the personality of the user have a significant bearing on the type of experience encountered. However, it is interesting to note that "bad trips" are infrequently reported (Hofmann and Hofmann, 1975). Only one report exists on the occurrence of "flashbacks" attributable to inhalant abuse (Kramer and Pierpaoli, 1971).

PHARMACOLOGY AND TOXICOLOGY

The chemicals found in most inhalants are rapidly absorbed into the respiratory system and passed through the blood to the brain (Comstock and Comstock, 1977; Wood and Weis, 1978). The central nervous system is effected by these substances which can be of a stimulant or depressant nature. Some products contain a variety of solvents – stimulants and depressants effecting the CNS with both actions simultaneously, (Aviado, 1978). Prockop (1978), for example, reported seven young men using a lacquer thinner containing eleven different solvents.

Since solvents are fat soluble, it is theorized that the nerve cell membrane (myelin) is effected, causing incomplete neural transmissions (Prockop and Couri, 1977). This results in an intoxicated state similar to alcoholic intoxication. Presently it is unknown if repeated exposure to these lipophilic vapors results in the accumulation of the substances and subsequent damage to cells in the brain (Comstock and Comstock, 1977; Berry et al., 1978). It should be noted that repeated use for some users amounts to several years. One individual cited (Comstock and Comstock, 1977) had an eleven year history of inhalant abuse.

The toxicity of the inhalants listed in Table I is difficult to determine. The deliberate inhalation of solvents is a unique use of the substances contained in many common consumer products. Aside from the anaesthetic agents, they have no medical treatment application. Two recent studies warn of solvent combinations which could potentate the toxicity of the chemical components (Couri and Abdel-Rahmen, 1978; Ikeda, 1978). These chemicals are not required to be pure and the potential hazard posed by these impurities are unknown. Dr. Charles W. Sharp (1977) describes the problem involved in determining the toxicity of the chemicals contained in the abused inhalants:

> "... over the long term, some chemicals will be absorbed at a level below that of producing an altered state but yet could well be contributing to a toxic reaction because of their water solubility, metabolism, and/or other properties. With all the possibilities of different chemical, physiological, and physical interactions, it is difficult to summarize the potential toxicities even when the retention, metabolism, and excretion of each of the individual components are known." (p. 241)

In addition, the available scientific data is based on the industrial exposure to these substances. The effects resultant from a five to seven hour day, five days a week, low concentration exposure are difficult to equate to the effects of brief, high concentration exposure experienced by the deliberate abuser. The toluene exposure experience during a typical glue-sniffing episode is estimated as fifty times the allowable industrial concentration (STASH, 1974.)

• Selected Toxicity Studies of Effected Areas

Kidney and Liver:

Results of a recent study conducted by Zimmerman et al. (1975) on patients suffering from advanced kidney failure indicate a relationship between the inhalation of hydrocarbons and kidney damage. Kidney and liver injury have been linked to toluene inhalation (O'Brien et al., 1971; Taher et al., 1974; Peterson and Bruckner, 1978); trichloroethylene, in particular, has been identified in cases of acute renal and hepatic damage (Baerg and Kimberg, 1970). Gasoline has also been implicated in hepatic injury due to its hydrocarbon content (Carroll and Abel, 1973). The tetraethyl lead content has been known to cause

anemia (Law and Nelson, 1968) and serious nerve abnormalities (Cohen, 1979).

Blood:

Hematological damage, including leukemia can be caused by the inhalation of solvents (Aksoy et al., 1972; Hayden et al., 1976). Benzene is frequently cited as the causal agent since it is known to damage the bone marrow, the production center for blood cells (Baselt, 1978).

Heart:

Cardiac sensitization was suggested as the cause of one death from gasoline sniffing (Poklis, 1975). Dr. Mildred Bass (1970) reported one hundred and ten "sudden sniffing deaths". SSD is the result of cardiac arrhythmia precipitated by physical or stressful activity following solvent sniffing. The fluorocarbons were cited in the majority of cases of SSD.

Brain:

In addition to the physiological damage, peripheral nervous system and central nervous system injury have been reported due to hydrocarbon exposure (Prockop, 1978). Two recent studies report mental impairment resultant from chronic inhalant abuse (Berry et al., 1978; Korman et al., 1978).

- **Future Research**

The recent trend toward the abuse of metallic paint aerosols suggests a need for further toxicity research, not only of the propellant gases and their chemical components but also of the metallic content. The zinc and copper absorption in three subjects studied was significant cause for concern (Wilde, 1975). Other areas suggested for future research include the carcinogenic (Capurro, 1976) and teratogenic (de la Garza Gutierrez et al., 1978b) potential of inhalants.

TOLERENCE AND DEPENDENCE

Tolerance is uniformly developed by most chronic users, particularly when glues or cement containing toluene are the preferred products. It is unclear how long it takes to develop a tolerance, however, one report cites a case where weekly usage for only three months resulted in a tolerance. After three years, another adolescent had to use eight tubes of plastic cement to induce the same effects earlier obtained from only one tube (Press & Done, 1967).

Although psychological dependence is frequently experienced there is little evidence of physiological dependence. Some researchers have observed withdrawal symptoms similar to delirium tremens (Merry & Zachariadis, 1962) and an abstinence syndrome characterized by headaches, pains in the abdomen and leg cramps (de la Garza Gutierrez et al., 1978a). Comstock and Comstock (1977) present a summarization of case abstracts of individuals practicing inhalant abuse, several claiming physiological dependence.

RECOMMENDATIONS

The difficulities in the diagnosis and treatment of the effects of inhalant use are exacerbated by the paucity of medical information on the subject. Dr. Leon Prockop recommends an extensive neurological evaluation, supplemental to an admission medical examination, to facilitate treatment assessment (see Appendix to Prockop, 1977). Long term follow-up examinations should also be provided, if possible, to determine the extent of pathological changes resultant from inhalant abuse. Given the diversity of inhalants used, categorization according to inhalant used might aid the identification of toxicity indigenous to specific substances.

Presently, many drug abuse treatment centers are ill-prepared to receive those suffering the effects of solvent inhalation. Personnel training should be provided to assure a knowledgeable and sensitive response to the specialized concerns of inhalant abusers. Although recidivism is high, supportive therapy is thought to be important to successful rehabilation programs (Arroyo, 1978; Campuzano, 1978). Users need to rebuild their self-image and experience a new environment with support and role models provided. Institutionalization is the subject of controversy, as evidenced by these conflicting opinions:

> "... forced abstinence alone is of no lasting value, and ... the approach to the individual must be a therapeutic, rather than a punitive, one. Thus, the greatest benefit of any legislation aimed at the abuses *per se*, aside from a highly questionable deterrent value, would seem to lie in its providing a mechanism whereby treatment of habitual offenders is encouraged." (Press & Done 1967, p. 167)

> "... inhalant users have a serious psychopathic behavior. They can best be cared for in institutions with tight security, as demonstrated in other countries ... Institutions equipped to care for them are a combination of a hospital with a prison type of control." (de Francisco et al., 1978, p. 402)

Cooperation from industry is also suggested. In response to reports of widespread glue-sniffing, the Testor Corporation added oil of mustard (allyl isothiocyanate) to its glue and plastic cement products. The nasal irritation caused by this chemical was hoped to deter abuse. Whether it was successful as a deterrent is unclear, however, subsequent studies pointed out the hazards of employing such additives without adequate prior testing. The decompostion rate was rapid; it proved to be a carcinogen in studies with rats; coronary thrombosis reportedly afflicts heavy mustard consumers; and, under certain conditions, cyanide fumes are created from allyl isothiocyanate (Fernandez, 1978).

Adolescence is a difficult period of adjustment to life. The solvent abuser from a low-socioeconomic background and her/his middle class counterpart both express boredom and feelings of hopelessness as contributing factors to their problem. More motivational, pharmacological, and toxicological data must be obtained in order to better understand the complexity of the problem. Inhalant abuse, as with other forms of drug abuse, does not lend itself to a simplistic resolution.

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1. Cox, Terrence C., Michael R. Jacobs, A. Eugene Leblanc, and Joan A. Marshman. *Drugs and Drug Abuse: A Reference Text*. Toronto: Addiction Research Foundation, 1983.

2. Duncan, David and Robert Gold. *Drugs and the Whole Person;* New York: John Wiley and Sons, 1982

3. Gilman, Alfred Goodman, Louis S. Goodman, and Alfred Gilman, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics;* 6th ed. New York: Macmillan Publishing Company, Inc., 1980.

4. Johnston. Lloyd D., Ph.D., Jerald G. Bachman, Ph.D., and Patrick M. O'Malley, Ph.D. *Highlights from Student Drug Use in America: 1975-1980*. University of Michigan Institute for Social Research. DHHS Publication No. (ADM) 81-1066. Rockville, Md.: National Institute on Drug Abuse, 1980.

5. Mason, Terry. *Inhalant Use and Treatment*. Research Monograph Series. DHEW Publication No. (ADM) 79-783. Rockville, Md.: National Institute on Drug Abuse, 1979.

6. Schlaadt, Richard G. and Peter T. Shannon. *Drugs of Choice: Current Perspectives on Drug Use*. Englwood Cliffs, N.J.: Prentice-Hall,Inc., 1982.

7. Sharp, Charles W., Ph.D. and Mary Lee Brehm, Ph.D., eds. *Review of Inhalants: Europhia to Dysfunction*. Research Monograph No. 15. DHEW Publication No. (ADM) 77-553. Rockville, Md.: National Institute on Drug Abuse, 1977.

8. ------- and L. Thomas Carroll, eds. *Voluntary Inhalation of Industrial Solvents*. DHEW Publication No. (ADM) 79-779. Rockville, Md.: National Institute on Drug Abuse, 1978.

ARTICLES:

Nitrous Oxide

1. Atkinson, Roland M.,M.D., Pius Morozumi, M.D., J. DeWayne Green, B.S., and John C. Kramer, M.D.; "Nitrous Oxide Intoxication: Subjective Effects in Healthy Young Men"; *Journal of Psychedelic Drugs* (now *Journal of Psychoactive Drugs*); 9(4); Oct.-Dec., 1977; p. 317-328.

   Article presents brief overview of anecdotal and controlled reports of subjective nitrous oxide effects, followed by authors' comparative study of high and low dose intoxication in 88 men. Authors develop profiie of typical reactions described by 80% of subjects, and 13 typical adverse reactions described by 20% of subjects. Study demonstrated nitrous oxide produces complex psychoactive experience characterized by euphoria, dreamy detachment, changes in body image, altered time perception, and awareness of reduced cognitive-motor proficiency. Adverse effects include nausea and anxiety. Authors conclude subanesthetic nitrous is safe and useful as laboratory tool, yet satisfies pleasure-producing criterion for abuse potential. 46 references.

2. Helisten, Carmen; "Nitrous Oxide's A Gas"; *The PharmChem Newsletter;* 4(5); May, 1976.

   Review of discovery and initial medical use between 1772 and 1868. Discusses actions and effects as mild anesthetic in minor surgery and details reported subjective effects of non-medical use, including euphoria, giddiness, excitement, reduced pain and depression, and hallucinations. Potential hazards of non-medical use reviewed: frozen lips and throat from inhaling directly from a tank or balloon, oxygen deprivation, nausea, disorientation, and occasional death with repeated, sustained use.

3. "Here's the Topper: Whipped-Cream Cans May be Fatal to N_2O Abusers"; *Medical World News;* April 16, 1979; p. 16.

   Six reported suffocation deaths from inhalation of nitrous oxide from whipped cream cannisters or legally-available "whippets" containing the anesthetic gas.

4. "N_2O Safe, but Dispensers Add Toxins"; *High Times;* October 1978; p. 12.

Response to reader question noting that commercial whipped cream and propellant cannisters contain over 20 contaminant chemicals in addition to N2O, three of which are known to produce nerve damage in humans.

5. "Nitrous Oxide Hazards"; *FDA Drug Bulletin;* 10(2); July, 1980.

Overview of animal and human research suggesting potential dangers of chronic N_2O inhalation, including effects on cellular division, impairment of vitamin metabolism, reduced testicular function in rats, possible death from oxygen inhalation, and development of a sustained use nervous system syndrome characterized by loss of balance, impotence, and leg weakness.

6. "Teratogenicity of Nitrous Oxide"; *FDA Drug Bulletin;* 11(1); March, 1981.

FDA advisory warning that findings from animal studies indicate occupational exposure to nitrous oxide or use of gas as an anesthetic during pregnancy may increase risks of spontaneous abortion and birth defects.

Amyl and Butyl Nitrite

1. Bennetts, Leslie; "Butyl Nitrite, a Popular Mind-Altering Drug, is Legal and Proliferating"; *New York Times;* November 21, 1978.

Describes legal, fast-buck butyl market, catering to an increasingly diverse national clientele, with commentary by manufacturers, vendors, and users. Regulatory efforts so far hindered by few adverse consequences of use other than headache, occasional nauseau, and faintness.

2. Cohen, Sidney, M.D.; "Amyl Nitrite Rediscovered"; *Drug Abuse and Alcoholism Newsletter;* 7(1); January, 1978.

Overview of nitrite actions and effects and current toxicological data, including build up of tolerance and certain adverse reactions (nausea, dizziness, weakness, flushing). Author notes amyl's reputation as an aphrodisiac and psychic stimulant among recreational users versus unpleasant effects generally ascribed by prescription users.

3. Finke, Harry B.; "Snappers"; *PharmAlert;* 8(2); Student Committee on Drug Abuse Education, University of Maryland, School of Pharmacy; December, 1976.

Administered since late-1800s in treatment of angina pectoris, increased use of amyl nitrite as an aphrodisiac and recreational drug in the 1960s led to its regulation as a prescription medication. Article examines street use and short-and long-term actions and effects, from relaxation of smooth muscles, cardiovascular acceleration, and facial flushing, to headache and dizziness.

4. Latimer, Dean; "The O.T.C. Taste Test: High Times Rates the Legal Highs"; *High Times;* 77; January, 1982; p. 41-43.

Sampling and staff commentary on a selection of over-the-counter psychoactive substances, including butyl nitrite and nitrous oxide.

5. Lowry, Thomas P., M.D.; "Psychosexual Aspects of Volatile Nitrites"; *Journal of Psychoactive Drugs;* 14(1-2); January-June, 1982; p. 77-79.

Examination of amyl/butyl nitrite use as sexual enhancers and aphrodisiacs. Author notes nitrites may be "the nearest thing to a true aphrodisiac," and describes current use among homosexual and heterosexual groups. Cautions that while few instances of nitrite-related hospital emergencies have been reported with inhalation of the drugs, ingestion or injection could produce severe adverse reactions or death.

6. Marmor, Michael, *et al*; "Risk Factors for Kaposi's Sarcoma in Homosexual Men"; *The Lancet;* 8281; May 12, 1982; p. 1083-1086.

Examination of possible role of amyl/butyl nitrite in recent outbreak of Acquired Immunodeficiency Syndrome (AIDS) among homosexual men.

7. Sigell, Leonard T., Ph.D., Frederick T. Kapp, M.D., Gregg A. Fusaro, E. Don Nelson, Pharm.D., and Russell S. Falck; "Popping and Snorting Volatile Nitrites: A Current Fad for Getting High"; *American Journal of Psychiatry;* 135(10); October, 1978; p. 1216-1218.

Examines individual expectations and social context in non-medical use of amyl and butyl nitrite: To expand creativity, to promote sense of abandon and enhance musical appreciation for discotheque devotees, and to intensify sexual experiences, primarily among homosexual men. Authors note that sales of butyl were estimated at over $%0 million per year, and that while evidence of harmful health effects is slim, nitrites may be found to produce cancer-causing nitrosamines in the body.

Solvents

1. Brecher, Edward M. and the Editors of Consumer Reports; "How to Launch a Nationwide Drug Menace"; in *Licit and Illicit Drugs;* Boston: Little, Brown and Company, 1972; p. 321-334.

Role of national media in popularizing glue-sniffing during 1960s. Authors note total absence of information on glue-sniffing prior to 1959, and the sudden explosion in media coverage—and adolescent use—following sensationalized reports of two Denver, Colo., sniffers that year. Authors argue that stories carrying explicit details of which commercial products produce psychoactive effects and how to sniff them created a glue-sniffing epidemic among American youth.

2. Christ, David; "Inhalation of Aerosol Propellants";*PharmAlert;* 11(2); Student Committee on Drug Abuse Education, University of Maryland, School of Pharmacy; April-June, 1980.

Examination of "sudden sniffing death" syndrome related to inhalation of aerosols containing flurocarbons (hairsprays, deodorants, frying pan lubricants, etc.), including chemistry, metabolism, and toxic effects on heart. 11 references.

3. Cohen, Sidney, M.D.; "Abuse of Inhalants"; in *Drug Abuse: Clinical and Basic Aspects;* Sachindra N. Pradhan, M.D., Ph.D., and Samarendra N. Dutta, M.D., Ph.D., eds.; Saint Louis: C.V. Mosby Company, 1977.

Overview of inhalants, including examination of history, prevalence, occurrence in commercial products, usage techniques, tolerance, toxicity, and rehabilitation. Author notes lack of solid investigation into spread of use within a community and difficulties in controlling inhalation of widely-available commercial solvents. 48 references.

4. Epstien, Merrill H., M.D., and William F. Wieland, M.D.; "Prevalence Survey of Inhalant Abuse"; *The International Journal of the Addictions;* 13(2); 1978; p. 271-284; rpt. by DHEW Public Health Service, 1979.

Random, household survey to assess levels of adolescent inhalant use was conducted in Atlanta housing project. Study design matched use with individual demographics (average age, sex, duration of use, age of onset, school grade level), juvenile arrests, degree of family organization, and other drug use. Findings included: children able to obtain commercial inhalants despite laws regulating sales to minors, the majority of inhalant users also used other drugs and alcohol at a higher rate than non-sniffing peers, and users had higher school dropout rates and more extensive criminal records than non-users.

5. Garriott, J., Ph.D., and C.S. Petty, M.D.; "Death from Inhalant Abuse: Toxicological and Pathological Evaluation of 34 Cases"; *Clinical Toxicology;* 16(3); 1980; p. 305-315.

Evaluation of "sudden sniffing death" syndrome in 34 inhalant-related deaths. Authors note that aerosols containing Freon comprised one-half of recorded inhalant deaths from sudden cardiac depression. 12 references.

6. Korman, Maurice Frank Trimboli, and Ira Semler; "A Comparative Evaluation of 162 Inhalant Users"; *Addictive Behaviors;* 5; 1980; p. 143-152.

Study of inhalant users admitted to Dallas hospital emergency rooms over a two year period. Inhalant group exhibited more aggressive behavior against self and others, higher incidence of cognitive deficits, and long-standing personality disorders and other drug dependence.

7. Novak, Allen and the STASH Staff; "The Deliberate Inhalation of Volatile Solvents"; *Journal of Psychedelic Drugs* (now *Journal of Psychoactive Drugs*); 12(2); April-June, 1980; p. 105-122.

Comprehensive review of current research on full range of inhalable substances and solvents, including discussion of prevalence and patterns of use, routes of administration, pharmacology and toxicity, tolerance and dependence, and subjective and psychological effects. 151 references.

8. Lewis, Jonathan D., M.D., Dennis Moritz, M.S., and Linda P. Mellis, M.A.; "Long-Term Toluene Abuse"; *American Journal of Psychiatry;* 138(3); March, 1981; p. 368-370.

Report of two cases of long-term glue sniffing (14 and 18 years), one subject suffering significant and irreversible brain damage, and the second evidencing progressive neurological damage and disturbed, psychotic behavior. Authors note that chronic glue sniffing is a relatively rare occurence.

9. Toutant, Claire and Steven Lippmann; "Fetal Solvents Syndrome"; *The Lancet;* 8130; June 23, 1979; p. 1356.

Case report of a newborn exhibiting symptoms of fetal alcohol syndrome (facial abnormalities, physical defects, poor responses, and possible cognitive deficits) where the mother had a 14-year history of daily, heavy solvent (primarily toluene) use.